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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,051	10/28/2003	Su Chen	034827-2601	5893
30542 7590 11/05/2009 FOLEY & LARDNER LLP P.O. BOX 80278 SAN DIEGO, CA 92138-0278			EXAMINER WEISZ, DAVID G	
			ART UNIT 1797	PAPER NUMBER
			MAIL DATE 11/05/2009	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/696,051

**Applicant(s)**

CHEN, SU

**Examiner**

DAVID WEISZ

**Art Unit**

1797

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 31 August 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-4, 6-17 and 30-56 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-17 and 30-56 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB08)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_
- Paper No(s)/Mail Date \_\_\_\_\_

### **DETAILED ACTION**

1. Acknowledgement is made of amendment filed 8/31/09. Upon entering the amendment, claims 1, 30 and 52 are amended.
2. Claims 1-4, 6-17 and 30-56 are pending and presented for examination.

### ***Response to Amendment***

3. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn. In response to applicant's remarks, the examiner modifies the grounds for rejection.

### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-4, 6-17 and 30-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The examiner respectfully reminds the Applicants that according to MPEP §2163:

#### **"2163.02. Standard for Determining Compliance with Written Description Requirement:**

The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she

was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

The specification does not disclose the following subject matter of claims 1, 9, 30 and 37 highlighted with bold font:

**Measuring the amount of unlabeled organic acids and oxygen-18 organic acids in the processed sample.**

While the specification provides a method of using mass spectroscopy to measure the organic acid, there is nothing in the specification that would lead one having ordinary skill in the art to use any other method of detection.

Thus, the Applicants did not show possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

7. Claims 1-4, 6-17 and 30-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for measuring an amount of unlabeled organic acid and oxygen-18 organic acid using mass spectroscopy, it does not enable any other method of measurement of these organic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. See claims 1, 9, 30 and 37, and specification, paragraphs [0016-0017]. Leis et al. (*J. Chromatogr. B*, 2003) discloses a method for detecting oxygen-18 labeled VPA using mass spectroscopy, however there is no indication for the success of the apparatus or method in terms of a detection route. Therefore, it would require undue experimentation for a routineer in the art to perform the method in the scope of the claims using an arbitrary detection/measurement means.

#### ***Claim Rejections - 35 USC § 102***

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

9. **Claims 1-3, 7-9 and 12-15** are rejected under 35 U.S.C. 102(a) as being anticipated by Leis et al. (*J. Chrom. B*, 2003) (Leis).

Leis discloses a method of measuring the amount of an unlabeled organic acid in a sample comprising, adding oxygen-18 labeled valproic acid (VPA) to sample suspected of containing the unlabeled VPA (2.5 Analytical method validation), processing the sample (2.5 Analytical method validation), measuring the labeled and unlabeled VPA via GC-MS analysis (2.5 Analytical method validation and 3.3 Mass spectrometry) and using the labeled acid to adjust the unlabeled measurement to reflect the true

amount of unlabeled organic acid originally present in the sample (2.5 Analytical method validation) (*claim 1, 2, 3, 9, 14, 15*). Processing results in an enrichment and chemical modification of the unlabeled organic acid in the sample, as it is inherent in the chromatography and mass spectrometry processes (*claims 7, 8, 12 and 13*).

### ***Claim Rejections - 35 USC § 103***

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. **Claims 4, 6, 16 and 17** are rejected under 35 U.S.C. 103(a) as being unpatentable over Leis in view of Nguyen et al. (US 2005/0070023) (Nguyen).

Leis does not disclose that the mass spectroscopy is LC-GS or that the sample is a urine sample.

Nguyen discloses a method of analyzing oxygen-18 labeled carboxylic acids by LC-MS [0004] (*claim 4 and 16*), and that the carboxylic acids are available in a urine sample [0003] (*claims 6 and 17*). It would have been obvious to one having ordinary skill in the art to use LC-MS in the method of Leis because it is a very well known method of quantitative analysis of such compounds. It would have been obvious for the sample of Leis to be a urine sample because organic acids are found in biological fluids, such as a urine sample.

13. **Claims 10, 11 and 46-56** are rejected under 35 U.S.C. 103(a) as being unpatentable over Leis in view of Nguyen, as applied to claims 4, 6, 16 and 17 above, and further in view of Shaw et al. (US 5686311) (Shaw).

Leis-Nguyen disclose determining levels of carboxylic acids in analytical samples using GC-MS is at its highest accuracy when stable isotope analogs (e.g. oxygen-18) are used as internal standards (Nguyen [0004-0005]). The references do not specifically disclose that multiple labeled organic acids are added to the sample.

Shaw discloses a method of diagnosing autism via a measurement of at least 3 (*claims 10-11, and 54-56*) of hydroxyl mono-acid, dihydroxy mono-acid (*claim 46*), dicarboxyl organic acid (*claim 47*), hydroxyl dicarboxyl acid (*claim 48*), tricarboxyl acid (*claim 49*), glycine conjugate (*claim 50*), glyoxylic acid (*Claim 51*), 4-hydroxyphenylacetic acid (*claim 52*) keto acid (*claim 53*) via GC-MS (Columns 2 and 3). It would have been obvious to one having ordinary skill in the art to add labels of each of these organic acids because it increases accuracy of GC-MS.

14. **Claims 30-45** are rejected under 35 U.S.C. 103(a) as being unpatentable over Leis in view of Nguyen and Shaw, as applied to claims 10, 11 and 46-56 above, and further in view of Breakefield et al. (US 5030570) (Breakefield).

Leis-Nguyen-Shaw disclose a method of diagnosing autism by determining levels of carboxylic acids in urine using oxygen-18 labeled organic acids as internal standards. The references disclose that GC-MS or LC-MS (Nguyen [0004-0005]) (*claims 31-35, 40-44*) can be used to determine multiple unlabeled organic acids in urine (Nguyen [0003]) (*claim 36 and 45*), with its accuracy enhanced by using multiple oxygen-18 labeled internal standards (Shaw, Columns 2 and 3) (*claims 38 and 39*). However, the references do not disclose that this method extends to diagnosing a metabolic defect, as disclosed in claims 30 and 37.

Breakefield discloses that organic acids, such as VMA, HVA and MHPG, are reduced substantially in the urine of people having a specific metabolic defect. It would have been obvious to one having ordinary skill in the art to extend the Leis-Nguyen-Shaw method to detect a metabolic defect, as the same method would be used to make such a determination (*claim 30 and 37*).

***Response to Arguments***

15. Applicant's arguments with respect to claims 1-4, 6-17 and 30-56 have been considered but are moot in view of the new ground(s) of rejection.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID WEISZ whose telephone number is (571)270-7073. The examiner can normally be reached on Monday - Thursday, 7:30 a.m. - 5:00 p.m., EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on (571)272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

11/3/2009

/Yelena G. Gakh/  
Primary Examiner, Art Unit 1797

/D. W./

Examiner, Art Unit 1797